

CLAIMS

1. A composition for maintaining the expansion, pluripotency, or self-replication ability of a stem cell, comprising active
5 STAT5.
2. A composition according to claim 1, wherein the stem cell is a hematopoietic stem cell.
- 10 3. A composition according to claim 1, wherein the active STAT5 is active STAT5A or active STAT5B.
4. A composition according to claim 1, wherein the active STAT5 is active STAT5A.
- 15 5. A composition according to claim 1, wherein the active STAT5 is:
- (a) a polypeptide consisting of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8, or a fragment
20 thereof;
 - (b) a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8 having at least one mutation selected from at least one amino acid substitution, addition and deletion, and having biological activity;
 - 25 (c) a polypeptide encoded by an allelic variant of a base sequence set forth in SEQ ID NO:1, 3, 5 or 7;
 - (d) a polypeptide which is a species homolog of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8;
or
 - 30 (e) a polypeptide having an amino acid sequence having at least 70% identity to any one of the polypeptides (a) to (d), and having biological activity; and
wherein in the active STAT5, at least one serine,

- 127 -

threonine, or tyrosine residue is phosphorylated.

6. A composition according to claim 1, wherein the active STAT5 is a homodimer or a heterodimer of:

5 (a) a polypeptide consisting of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8, or a fragment thereof;

(b) a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8 having at least one mutation selected from at least one amino acid substitution, addition and deletion, and having biological activity;

(c) a polypeptide encoded by an allelic variant of a base sequence set forth in SEQ ID NO:1, 3, 5 or 7;

10 (d) a polypeptide which is a species homolog of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8; or

(e) a polypeptide having an amino acid sequence having at least 70% identity to any one of the polypeptides (a) to (d), and having biological activity.

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7. A composition according to claim 1, wherein in the active STAT5, a tyrosine residue at position 694 in SEQ ID NO:2 or a tyrosine residue corresponding thereto is at least phosphorylated.

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8. A composition according to claim 1, wherein the active STAT5 is a dimer.

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9. A composition according to claim 1, wherein the active STAT5 has an amino acid residue substitution in at least one position selected from the group consisting of position, 150, 298, and 710 in SEQ ID NO:2 or 6.

10. A composition according to claim 1, wherein in the active STAT5, a histidine residue at position 298 and/or a serine residue at position 710 in SEQ ID NO:2 or 6, or residues corresponding thereto, are substituted with arginine and/or phenylalanine, respectively.
11. A composition according to claim 1, wherein in the active STAT5, a glutamic acid residue at position 150 and/or a serine residue at position 710 in SEQ ID NO:2 or 6, or residues corresponding thereto, are substituted with glycine and/or phenylalanine, respectively.
12. A composition according to claim 1, wherein in the active STAT5, a serine residue at position 710 in SEQ ID NO:2 or 6 is substituted with phenylalanine.
13. A composition according to claim 1, wherein the active STAT5 has an amino acid sequence set forth in SEQ ID NO:10 or 13.
14. A composition according to claim 1, wherein the active STAT5 is consistently active or transiently active.
15. A composition according to claim 1, further comprising a cellular physiologically active substance.
16. A composition according to claim 15, wherein the cellular physiologically active substance is selected from the group consisting of SCF, TPO, and Flt-3L.
17. A composition according to claim 15, wherein the cellular physiologically active substance contains SCF, TPO, and Flt-3L.

18. A composition according to claim 1, further comprising a pharmaceutically acceptable carrier.

5 19. A composition for maintaining the expansion, pluripotency, or self-replication ability of a stem cell, comprising STAT5 and an agent capable of activating STAT5.

10 20. A composition according to claim 19, wherein the STAT5 is:

(a) a polypeptide consisting of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8, or a fragment thereof;

15 (b) a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8 having at least one mutation selected from at least one amino acid substitution, addition and deletion, and having biological activity;

(c) a polypeptide encoded by an allelic variant of a base sequence set forth in SEQ ID NO:1, 3, 5 or 7;

20 (d) a polypeptide which is a species homolog of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8; or

25 (e) a polypeptide having an amino acid sequence having at least 70% identity to any one of the polypeptides (a) to (d), and having biological activity.

30 21. A composition according to claim 19, wherein the STAT5 activating agent is a member selected from the JAK family or a variant thereof.

22. A composition for maintaining the expansion, pluripotency, or self-replication ability of a stem cell, comprising a nucleic acid molecule encoding active STAT5.

23. A composition according to claim 22, wherein the nucleic acid molecule encoding active STAT5 contains a nucleic acid sequence encoding STAT5 which forms a dimer.

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24. A composition according to claim 22, wherein the nucleic acid molecule encoding active STAT5 is:

(a) a polynucleotide having a base sequence set forth in SEQ ID NO:1, 3, 5 or 7 or a sequence fragment thereof;

10 (b) a polynucleotide encoding a polypeptide consisting of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8, or a fragment thereof;

(c) a polynucleotide encoding a variant polypeptide having an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8 having at least one mutation selected from the group consisting of at least one amino acid substitution, addition and deletion, and having biological activity;

15 (d) a polynucleotide which is an allelic variant of DNA consisting of a base sequence set forth in SEQ ID NO:2, 4, 6 or 8;

20 (e) a polynucleotide encoding a species homolog of a polypeptide consisting of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8;

(f) a polynucleotide encoding a polypeptide hybridizable to any one of the polynucleotides (a) to (e) under stringent conditions, and having biological activity; or

25 (g) a polynucleotide consisting of a base sequence having at least 70% identity to any one of the polynucleotides (a) to (e) or a complementary sequence thereof, and having biological activity.

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25. A composition according to claim 22, wherein the active

- 131 -

STAT5 has an amino acid residue substitution in at least one position selected from the group consisting of position, 150, 298, and 710 in SEQ ID NO:2 or 6.

5 26. A composition according to claim 22, wherein in the active STAT5, a histidine residue at position 298 and/or a serine residue at position 710 in SEQ ID NO:2 or 6, or residues corresponding thereto, are substituted with arginine and/or phenylalanine, respectively.

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27. A composition according to claim 22, wherein in the active STAT5, a glutamic acid residue at position 150 and/or a serine residue at position 710 in SEQ ID NO:2 or 6, or residues corresponding thereto, are substituted with glycine and/or phenylalanine, respectively.

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28. A composition according to claim 22, wherein in the active STAT5, a serine residue at position 710 in SEQ ID NO:2 or 6 is substituted with phenylalanine.

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29. A composition according to claim 22, wherein the active STAT5 has an amino acid sequence set forth in SEQ ID NO:10 or 13.

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30. A composition according to claim 22, wherein the nucleic acid molecule is contained in a vector.

31. A composition according to claim 22, wherein the nucleic acid molecule is contained in a retrovirus vector.

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32. A composition according to claim 22, wherein the nucleic acid molecule has a sequence set forth in SEQ ID NO:9.

33. A composition for expanding a stem cell, comprising a nucleic acid molecule encoding STAT5 and an agent capable of activating the STAT5.

5 34. A composition according to claim 33, wherein the nucleic acid molecule encoding active STAT5 is:

(a) a polynucleotide having a base sequence set forth in SEQ ID NO:1, 3, 5 or 7 or a sequence fragment thereof;

10 (b) a polynucleotide encoding a polypeptide consisting of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8, or a fragment thereof;

15 (c) a polynucleotide encoding a variant polypeptide having an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8 having at least one mutation selected from the group consisting of at least one amino acid substitution, addition and deletion, and having biological activity;

(d) a polynucleotide which is an allelic variant of DNA consisting of a base sequence set forth in SEQ ID NO:2, 4, 6 or 8;

20 (e) a polynucleotide encoding a species homolog of a polypeptide consisting of an amino acid sequence set forth in SEQ ID NO:2, 4, 6 or 8;

25 (f) a polynucleotide encoding a polypeptide hybridizable to any one of the polynucleotides (a) to (e) under stringent conditions, and having biological activity; or

30 (g) a polynucleotide consisting of a base sequence having at least 70% identity to any one of the polynucleotides (a) to (e) or a complementary sequence thereof, and having biological activity.

35. A composition according to claim 33, wherein the nucleic acid molecule is contained in a vector.

36. A composition according to claim 33, wherein the nucleic acid molecule is contained in a retrovirus vector.

5 37. A composition according to claim 33, wherein the STAT5 activating agent is a member selected from the JAK family or a variant thereof.

38. A method for maintaining the expansion, pluripotency,
10 or self-replication ability of a stem cell, comprising the steps of:

- A) providing a stem cell; and
- B) providing active STAT5 to the stem cell.

15 39. A method for maintaining the expansion, pluripotency, or self-replication ability of a stem cell, comprising the steps of:

- A) providing a stem cell;
- B) providing STAT5 to the stem cell; and
- 20 C) activating the STAT5.

40. A method for preparing a stem cell in a predetermined quantity, comprising the steps of:

- A) providing a stem cell; and
- 25 B) providing active STAT5, or STAT5 and an agent capable of activating the STAT5, to the stem cell.

41. A cell, obtained by a method according to any one of claims 38 to 40.

30 42. Use of active STAT5 for maintaining the expansion, pluripotency, or self-replication ability of a stem cell.

43. Use of STAT5 for maintaining the expansion, pluripotency, or self-replication ability of a stem cell.
- 5 44. Use of STAT5 and an agent capable of activating the STAT5 for maintaining the expansion, pluripotency, or self-replication ability of a stem cell.
- 10 45. A cell, obtained by treating a stem cell with active STAT5, or STAT5 and an agent capable of activating the STAT5.
46. A tissue, obtained by a cell obtained by treating a stem cell with active STAT5, or STAT5 and an agent capable of activating the STAT5.
- 15 47. An organ, obtained by a cell obtained by treating a stem cell with active STAT5, or STAT5 and an agent capable of activating the STAT5.
- 20 48. A medicament composition, comprising a cell obtained by treating a stem cell with active STAT5, or STAT5 and an agent capable of activating the STAT5.
- 25 49. A method for treatment or prophylaxis of a disease or a disorder in need of a stem cell or a differentiated cell derived therefrom, comprising the steps of:
- A) administering to a subject in need of the treatment or prophylaxis a cell obtained by treating a stem cell with active STAT5, or STAT5 and an agent capable of activating the STAT5.
- 30 50. Use of a cell obtained by treating a stem cell with active STAT5, or STAT5 and an agent capable of activating the STAT5, for treatment or prophylaxis of a disease or a disorder in

need of a stem cell or a differentiated cell derived therefrom.

51. Use of a cell obtained by treating a stem cell with active
STAT5, or STAT5 and an agent capable of activating the STAT5,
5 for production of a medicament for treatment or prophylaxis
of a disease or a disorder in need of a stem cell or a
differentiated cell derived therefrom.